

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for proliferating human hepatocytes, which comprises transplanting human hepatocytes into ~~a~~the liver of an immunodeficient hepatopathy mouse and proliferating ~~the said transplanted~~ human hepatocytes in the ~~mouse liver~~ of said mouse, wherein the said mouse is:

(a) administered an effective amount of a complement inhibitor; or

(b) a progeniture mouse obtained by mating an immunodeficient hepatopathy mouse and a decay-accelerating factor (DAF/CD55) transgenic mouse,

wherein said mouse is protected against tissue damage associated with human complement produced by the human hepatocytes.

~~transplanted with the human hepatocytes is fed under such a condition as being protected from the attack by human complement produced by the human hepatocytes transplanted therein.~~

2. (Cancelled)

3. (Withdrawn) The method for proliferating human hepatocytes of claim 1, wherein the immunodeficient hepatopathy mouse is the progeniture mouse obtained by mating between a genetically immunodeficient mouse and a genetically hepatopathy mouse.

4. (Withdrawn) The method for proliferating human hepatocytes of claim 3, wherein the progeniture mouse is a hemizygous immunodeficient hepatopathy mouse.

5. (Withdrawn) The method for proliferating human hepatocytes of claim 4, wherein the hemizygous immunodeficient hepatopathy mouse is administered with a hepatocyte growth inhibitor and then the human hepatocytes are transplanted therein.

6. (Withdrawn) The method for proliferating human hepatocytes of claim 1, wherein the immunodeficient hepatopathy mouse transplanted with the human hepatocytes is administered with an anti-mouse Fas antibody.

7. (Original) The method for proliferating human hepatocytes of claim 1, wherein the human hepatocytes to be transplanted into the immunodeficient hepatopathy mouse are proliferative human hepatocytes.

8. (Currently Amended) The method for proliferating human hepatocytes of claim 7, wherein the proliferative human hepatocytes are human hepatocytes recognized by a monoclonal antibody which specifically recognizes human hepatocytes which proliferate ~~with forming~~ to form a colony.

9. (Original) The method for proliferating the human hepatocytes of claim 8, wherein the monoclonal antibody is one produced from Mouse-Mouse hybridoma K8223 (FERM BP-8334).

10. (Currently Amended) A method for large scale proliferation of ~~proliferating~~ human hepatocytes ~~in large scale~~, which comprises the following steps (1) to (3), and the steps (2) and (3) are repeated at least once;

- (1) a step comprising transplanting human hepatocytes into ~~a~~ the liver of an immunodeficient hepatopathy mouse, and then proliferating the transplanted human hepatocytes in the mouse liver;
- (2) a step of isolating the proliferated human hepatocytes from the mouse liver; and
- (3) a step comprising transplanting the human hepatocytes isolated from the mouse liver into the liver of an immunodeficient hepatopathy mouse, and then feeding the mouse transplanted with the human hepatocytes for not shorter than 50 days ~~under such a condition as being protected from the attack by human complement produced by the human hepatocytes,~~

wherein each of the mouse mice transplanted with the human hepatocytes in step (1) and step (3) is:

(a) administered an effective amount of a complement inhibitor; or

(b) a progeniture mouse obtained by mating an immunodeficient hepatopathy mouse and a decay-accelerating factor (DAF/CD55) transgenic mouse,

wherein said mice are protected against tissue damage associated with human complement produced by the human hepatocytes fed under such a condition as being protected from the attack by human complement produced by the human hepatocytes transplanted therein.

11. (Cancelled)

12. (Withdrawn) The method for proliferating human hepatocytes in large scale of claim 10, wherein the immunodeficient hepatopathy mouse in the step (1) and/or the step (3) is the progeniture mouse obtained by mating between a genetically immunodeficient mouse and a genetically hepatopathy mouse.

13. (Withdrawn) The method for proliferating human hepatocytes in large scale of claim 12, wherein the progeniture mouse is a hemizygous immunodeficient hepatopathy mouse.

14. (Withdrawn) The method for proliferating human hepatocytes in large scale of claim 13, wherein the hemizygous immunodeficient hepatopathy mouse is administered with a hepatocyte growth inhibitor and then human hepatocytes are transplanted therein.

15. (Withdrawn) The method for proliferating human hepatocytes in large scale of claim 10, wherein the immunodeficient hepatopathy mouse transplanted with human hepatocytes in the step (1) and/or the step (3) is administered with an anti-mouse Fas antibody.

16. (Currently Amended) The method for large scale proliferation of~~proliferating~~ human hepatocytes ~~in large scale~~ of claim 10, wherein the human hepatocytes to be transplanted into the liver of the immunodeficient hepatopathy mouse in the step (1) and/or the step (3) are proliferative human hepatocytes.

17. (Currently Amended) The method for large scale proliferation of~~proliferating~~ human hepatocytes ~~in large scale~~ of claim 16, wherein the proliferative human hepatocytes are human hepatocytes recognized by a monoclonal antibody which specifically recognizes human hepatocytes which proliferate ~~with forming~~ to form a colony.

18. (Currently Amended) The method for large scale proliferation of~~proliferating~~ human hepatocytes ~~in large scale~~ of claim 17, wherein the monoclonal antibody is one produced from Mouse-Mouse hybridoma K8223 (FERM BP-8334).

19. (Withdrawn) The method for proliferating human hepatocytes in large scale of claim 10, wherein only human hepatocytes are substantially isolated in step (2) by at least one of the following procedures (a) and (b);

- (a) to treat a liver tissue separated from the mouse liver with collagenase; and
- (b) to isolate cells being recognized by a monoclonal antibody which specifically recognizes human hepatocytes but not recognizes non-human hepatocytes.

20. (Withdrawn) The method for proliferating human hepatocytes in large scale of claim 19, wherein the monoclonal antibody is one produced by Mouse-Mouse hybridoma K8216 (FERM BP-8333).

21. (Withdrawn) A chimeric mouse having proliferated human hepatocytes in its liver, wherein the human hepatocytes are proliferated by the method for proliferating human hepatocytes of claim 1, or by the method for proliferating human hepatocytes in large scale of claim 10, wherein the proliferated human hepatocytes make up not less than 70% of the cells in the liver, and which exists not less than 60 days.

22. (Cancelled)

23. (Withdrawn) The chimeric mouse of claim 21, wherein said mouse has human-type P450 activity.

24. (Withdrawn-Currently Amended) A method for obtaining human hepatocytes, comprising isolating the human hepatocytes from the liver of the chimeric mouse of claim 21.

25. (Withdrawn) The method for obtaining human hepatocytes of claim 24, wherein only human hepatocytes are substantially isolated by at least one of the following procedures (a) and (b);
(a) to treat a liver tissue separated from the mouse liver with collagenase; and
(b) to isolate cells being recognized by a monoclonal antibody which specifically recognizes human hepatocytes but not recognizes non-human hepatocytes.

26. (Withdrawn) The method for obtaining human hepatocytes of claim 25, wherein the monoclonal antibody is one produced from Mouse-Mouse hybridoma K8216 (FERM BP-8333).

27. (Withdrawn) Human hepatocytes obtained by the method of claim 24.

28. (Withdrawn) A cellular kit containing the human hepatocytes of claim 27.

27. **29. (Withdrawn)** A hybrid-type artificial liver filled with the human hepatocytes of claim

30. (Withdrawn) A monoclonal antibody which specifically recognizes human hepatocytes proliferated in a mouse liver but does not recognize non-human hepatocytes.

31. (Withdrawn) The monoclonal antibody of claim 30, which is one produced from Mouse-Mouse hybridoma K8216 (FERM BP-8333).

32. (Withdrawn) Mouse-Mouse hybridoma K8216 (FERM BP-8333).

33. (Withdrawn) A method for testing pharmaceutical kinetics or toxicity of a candidate substance, which comprises systemically administering the substance into the chimeric mouse of claim 21 or 23.